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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,751	06/01/2001	Seo Young Jeong	GRT/912-25	4257

23117 7590 03/12/2007
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EXAMINER

SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
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1636

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 09/744,751	Applicant(s) JEONG ET AL.	
	Examiner Daniel M. Sullivan	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 December 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,5-13,22-27,29,30,40,42 and 44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 30 and 44 is/are allowed.
- 6) ☒ Claim(s) 1,3,5-13,22-27,29,40 and 42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is a reply to the Paper filed 26 December 2006 in response to the Non-Final Office Action mailed 24 August 2006. Claims 2, 4, 14-21, 31-39, 41, 43 and 45 were withdrawn from consideration and claims 1, 3, 5-13, 22-27, 29, 30, 40, 42 and 44 were considered in the 24 August Office Action. Claims 2, 4, 6, 14-21, 28, 31-39, 41, 43 and 45 were canceled and claims 1, 30, 40, 42 and 44 were amended in the 26 December Paper. Claims 1, 3, 5-13, 22-27, 29, 30, 40, 42 and 44 are pending and under consideration.

Response to Amendment and Arguments

Specification

Objection to the disclosure for the reasons set forth in the 24 August Office Action at page 2 is **withdrawn** in view of the amendment to the specification.

Claim Rejections - 35 USC § 112

Rejection of claim 40 under 35 U.S.C. 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **withdrawn** in view of the claim amendments.

Claim Rejections - 35 USC § 103

Rejection of claims 1, 3, 5, 7-13, 24, 26, 29, 30, 40 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (1997) WO 97/11682 is **withdrawn** in view of the amendment of the claims such that the non-triglyceride oil is limited to squalene or squalane.

Claim 1 **stands rejected** and claims 3, 5, 7-13, 24, 26, 29, 30, 40 and 42 are **newly rejected** (necessitated by amendment of the claims such that they require squalene or squalane) under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (*supra*), as applied to claim 1 herein above, in view of Hartounian et al. US Pub. No. 2002/0039596 (effective filing date 14 November 1997; previously made of record). This rejection is maintained for the reasons set forth in the 24 August Office Action at pages 7-9 and herein below in the response to arguments. It is further noted that the limitations of claims 3, 5, 7-13, 24, 26, 29, 30, 40 and 42 are found in the teachings of Liu et al. as described in the 24 August Office Action at pages 4-7.

Response to Arguments

In response to the *prima facie* rejection of record, Applicant urges, "Applicants found that the choice of oil component in o/w is very important in formulating emulsion-based drug or gene delivery systems, and that transfection activity was the highest when squalene or squalane is used as the oil component." (Page 9, first full paragraph.) Applicant further points out that the disclosure demonstrates that squalene emulsions showed higher transfection activity than soybean oil or linseed oil emulsions and that a squalene emulsion was the most stable with particles at any given emulsified concentration.

Applicant contends that the claimed invention is not obvious over the teachings of Liu et al. in view of Hartounian et al. because Liu and Hartounian do not teach or suggest the use of 2-30% neutral lipid in an emulsion as presently claimed.

This argument has been fully considered but is not deemed persuasive in view of the record as a whole. As stated in the 24 August Office Action at page 5, “Liu et al. teaches an oil-in-water lipid emulsion comprising a non-triglyceride oil and a cationic lipid transfection agent, wherein the range of oil and cationic lipid concentrations contemplated by Liu et al. overlap with the ranges recited in the instant claims. ‘In the case where the claimed ranges ‘overlap or lie inside ranges disclosed by the prior art’ a prima facie case of obviousness exists.’ *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). See MPEP 2144.05. In addition, it is recognized that, “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

For the reasons stated in the 24 August Office Action, it would have been obvious to one of ordinary skill in the art to use squalene as the oil component in the emulsion of Liu et al. in view of the teachings of Hartounian et al. and the record as a whole. Therefore, the claimed composition as a whole, including the concentration range recited in the claims, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant further asserts that neither document shows improved gene transfection efficiency or sizes stability and that such results are unexpected in view of the prior art.

This argument has been fully considered but is not deemed persuasive because, as discussed above, it would be obvious to make a composition comprising all of the elements of the claimed invention. Whatever advantage is obtained using squalene as the non-triglyceride oil is inherent to the composition. Mere recognition of latent properties in the prior art does not

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render nonobvious an otherwise known invention. *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

With regard to Applicant's assertion that the results would be unexpected, it is first noted that the submission is not a proper showing of unexpected results. MPEP 716.01 II. states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results..." MPEP 716.02(g) states, "The reason for requiring evidence in declaration or affidavit form is to obtain the assurances that any statements or representations made are correct, as provided by 35 U.S.C. 25 and 18 U.S.C. 1001.' Permitting a publication to substitute for expert testimony would circumvent the guarantees built into the statute. *Ex parte Gray*, 10 USPQ2d 1922, 1928 (Bd. Pat. App. & Inter. 1989)." Thus, the submission of a published document and attorney arguments cannot be accepted as evidence of unexpected results. Furthermore, there is no evidence of record that the smaller particle size and greater stability obtained with squalane and squalene is unexpected to a non-obvious extent. Any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, Tables 1-3 suggest an approximately 25% reduction in size relative to other oils, however, tables 10, 11 and 13 do not evidence any difference in particle size when squalene is used. Therefore, the record does not clearly evidence that the difference in size and stability is truly unexpected to a non-obvious degree.

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Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §103(a) as obvious over the art.

Rejection of claims 1, 22, 24 and 25 under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (*supra*), as applied to claims 1, 22 and 24 herein above, in view of Gao et al. (1996) *Biochem.* 35:1027-1036 is **withdrawn** in view of the amendment of the claims such that the non-triglyceride oil is limited to squalene or squalane.

Rejection of claims 1, 22, 23 and 27 under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (*supra*), as applied to claims 1 and 22 herein above, in view of Benz et al. (1996) WO 96/14864 is **withdrawn** in view of the amendment of the claims such that the non-triglyceride oil is limited to squalene or squalane.

New Grounds Necessitated by Amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 22, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (*supra*) in view of Hartounian et al. (*supra*), as applied to claims 1, 22 and 24 herein above, and further in view of Gao et al. (1996) *Biochem.* 35:1027-1036.

The limitations of claims 1, 22 and 24 and the teachings of Liu et al. in view of Hartounian et al. with regard thereto are discussed herein above and in the 24 August Office Action. Liu et al. in view of Hartounian et al. does not teach that the composition should comprise the cationic polymer polylysine.

Gao et al. teaches that the inclusion of polylysine in various cationic liposome formulations potentiates transfection of many different cell types. (See especially the section entitled "*Potentiation of Cationic Liposome-Mediated Transfection in Vitro by Polycations*" commencing on page 1029, Table 1, Figure 1 and the caption thereto).

It would have been obvious to one of ordinary skill in the art to modify the cationic liposome composition taught by Liu et al. to include polylysine as taught by Gao et al. according to the composition of the instant claims. Motivation to combine these teachings comes from the nature of the problem solved by the composition of Liu et al., which is to provide a delivery

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vehicle for introducing nucleic acids and other molecules into host cells, and the advantage of potentiated delivery obtained by including polylysine in cationic liposome compositions which is demonstrated by Gao et al. In view of the art, considered as a whole, one of ordinary skill would clearly perceive a benefit in modifying the composition of Liu et al. by the inclusion of polylysine.

Absent evidence to the contrary, one would have a reasonable expectation of success in combining the art in view of the fact that Gao et al. demonstrates enhancement of three distinct cationic liposome compositions by the inclusion of polylysine (see especially Fig. 1 and the caption thereto) and that enhancement was seen in a variety of cell types (see especially Table 1).

In view of the foregoing, the invention of claims 1, 22, 24 and 25 as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC §103(a) as obvious over the art.

Claims 1, 22, 23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (*supra*) in view of Hartounian et al. (*supra*), as applied to claims 1 and 22 herein above, and further in view of Benz et al. (1996) WO 96/14864.

The limitations of claims 1 and 22 and the teachings of Liu et al. in view of Hartounian et al. with regard thereto are discussed herein above and in the 24 August Office Action. Liu et al. in view of Hartounian et al. does not teach the composition comprising a targeting moiety.

Benz et al. teaches immunoliposomes that optimize internalization of a drug into target cells bearing a cell surface marker comprising a Fab' domain of an antibody that specifically binds to the characteristic marker. (See especially, the abstract, and the paragraph bridging pp. 4-

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5.) In the section entitled “(C) Fab’ Antibody Fragment” (see especially p. 20, ¶2), Benz et al. provides a variety of examples Fab’ molecules targeted to various cell surface receptors that would be expressed on many of the cells listed in the Markush group of claim 27.

It would have been obvious to one of ordinary skill in the art to modify the cationic liposome composition taught by Liu et al. to include a targeting molecule as taught by Benz et al. according to the composition of the instant claims. Motivation to combine these teachings comes from the nature of the problem solved by the composition of Liu et al., which is to provide a delivery vehicle for introducing nucleic acids and other molecules into host cells, and the advantage of optimized internalization of the liposome vehicle into target cells bearing a characteristic cell surface marker as taught by Benz et al. (See especially the Abstract.) In view of the art, considered as a whole, one of ordinary skill would clearly perceive a benefit in modifying the composition of Liu et al. by the inclusion of a targeting moiety.

Absent evidence to the contrary, one would have a reasonable expectation of success in combining the art in view of the demonstrated efficacy of Fab’ targeting demonstrated by Benz et al. (See especially Example 2.)

In view of the foregoing, the invention of claims 1, 22, 23 and 27 as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC §103(a) as obvious over the art.

Allowable Subject Matter

Claims 30 and 44 are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Daniel M Sullivan, Ph.D.
Primary Examiner
Art Unit 1636